Remarks

Claims 39, 43, and 46 are withdrawn as a result of the examiner's cited prior arts teaching all the limitation in these claims.

Claim 52 is rewritten in independent form incorporating all existing limitation to overcome the examiner's objection that it depends on a rejected claim. The language of the claim has also been changed (part e) to overcome the examiner's rejection due to vagueness under section 112.

Claim 55 is rewritten in its independent form incorporating all existing limitation. This claim was rejected by the examiner quoting Sexena uses of a counting device such as an Auto gama counter. Sexena's method was only possible at the time of the invention when used with two isotopes that emit different types of radiation such as beta radiation versus gamma radiation. Iodine-125 can emit gamma radiation (photon/ uncharged electromagnetic radiation) when Iodine-131 and other radioisotopes cited only emit beta radiation (electrons/ negatively charged particles) thus enable selective quantification by a gamma counter and a beta counter AKA an auto gamma counter. Selective screening was not the method that enables gamma and beta radiation differentiation by blocking different percentage of radiation from each isotope, but instead scintillation counting was used. Thus screening to enable selective quantification or beta radiation alone of different energy level is novel and non-obvious over prior arts. Applicant invention describes a method of differentiating two isotopes that only emit beta radiation which is in itself novel over Sexena's teaching.

This claim was further rejected by quoting Shuber et al. which teaches the hypothetical use of a **multi-orifice impedance counter**. This device is used for the purpose of counting beads (a non-radioactive substitute method) and **does not have anything to do with radioisotopes** (an understandable misinterpretation by the examiner). Further clarification will use the following sentence quoted from Shuber et al.

"While the following example uses radiolabeled nucleotides and an imager that detects the radioactive decay events, other methods of enumerating may be used, such as hybridization beads used in conjunction with a multi-orfice (sic) impedance counter."

The above sentence clearly stated that beads in conjunction with a multi-orifice impedance counter can be used to replace radiolabeled nucleotides and an imager that detects the radioactive decay events. In light of the new information provided here, applicant respectfully requests that the examiner reconsider the rejection of this particular claim.

Claim 79, 80, and 81 are added as dependent claims of claim 52 which was indicated by the examiner to be allowable if the objection and the 112 rejection are overcome. These claims are further depend on claim 55 which was requested for reconsideration above.

Claim 82 is a revision of Claim 54 which was rejected quoting that Shuber et al. teaches all the limitation. **Claim 82, further adds new limitations to accentuate the novel and non-obviousness of the claimed invention.** The inventive step here is no longer a method of distinguishing two radioactive isotopes in a mixture, but is a method of isolating the molecular differences between two samples through a systematic panning process using the ability to differentiate two isotopes in a mixture as an enabling means. Claim 82-89 encompass this panning process wherein two samples are labeled with two different radioactive isotopes, then mixed and undergone separation until some differences become apparent and can be identified. The panning process here should not be compared with the array display method where two samples of DNA are labeled with different fluorescent colors and displayed on the same array because:

- **The panning process allow subsequent steps so if no difference is found in the first separation, then further separation is possible while the array display method is a single step with no further separation possible.**
- **The array method works well with DNA; however, its success does not carry over to protein because of bulky fluorescent dyes used for labeling. The substitution of two radioactive isotopes for two fluorescent dyes thus is an enablement, but not an obvious step because others have failed to see**

> **that the substitution is possible and continued the futile effort of labeling proteins with fluorescent dyes for protein array analysis. (Zyomyx Inc. failed as a result of pursuing the fluorescent dye method)**

While teaching by Shuber et al can be interpreted to encompass all limitation in claim 50; the additional limitation added in claim 54 is completely different. **Shuber teaches a method of finding a DNA sequence change by using a specific probe for this sequence in combination with a probe for a constant sequence on one sample and then makes statistical comparison of the results with those of many other samples** (in Shuber's method, the analyst go after a specific DNA sequence and can only examine the difference in that DNA sequence only). **Applicant's invention emphasizes a method of isolating a difference between two samples without any preconception or bias of what the difference may be. Applicant's invention can yield totally unexpected differences between two samples not anticipated by the analyst thus is sufficient reason to overcome 102/103 rejection. Additionally, the teachings are not similar or equivalent or anticipated according to the way the new claim is rewritten.**

Claim 83, 84, 85, 86, 87, 88, and 89 are dependent claims of claim 82 that seek to claim further limitations. Cited prior arts do not teach any of these limitations in combination with claim 82 limitations.

Claim 90 is rewritten from claim 60 which incorporate the limitations for protein analysis only. Claim 60 and claim 58 that it depends on were rejected by the combine teaching of Brown et al. and Shuber et al. The combination of these two teaching are improper because:

(a) Brown et al. teaches the uses of radioactive isotopes; however, this is the use of one sample per array commonly known to those skilled in the art. There is no suggestion that two different isotopes can be used together on one array.

(b) Shuber at al. does not really teach the enablement of how two isotopes in a mixture can be distinguished, but merely suggests using their differences in emission spectra. One with ordinary skill in the art may be able to interpret this suggestion as distinguishing the different radioisotopes using their differences in scintillation spectra in a scintillation counter. As such scintillation counting can only be used to read individual sample and cannot be used for an array of samples in the micro array format. Furthermore, it would defeat the purpose of using a micro array if every single spot on an array must be removed and counted individually on a scintillation counter. Applicant teaches a screening method to selectively quantified different radioactive isotopes on the same array to overcome this technical problem which in itself is novel (see also remark for claim 55).

(c) Applicant claimed invention (now limited to just protein on protein array) **is non-obvious because labeling with two radioactive isotopes works while labeling with two fluorescent dyes does not work as well, but it was not apparent to Zyomyx Inc. which went bankrupt as a result of pursuing the fluorescent dyes method.**

applicant respectfully requests that the examiner reconsider this new claim.

Claim 91 is a dependent of claim 90 further seek a limitation that a screen is used to enable the determination of the ratio of each radioactive isotopes. With reference to claim 55, none of the cited reference teaches the use of a screen or equivalence to accomplish this goal. To the applicant knowledge, there has not been a device that uses the screening method to block higher proportion of one radioisotope to calculate the ratio of two radioisotopes in a mixture.

Claim 92 is a dependent claim of claim 90 further seeks a limitation that the difference in radioactive isotopes half-life is used to aid the determination of the ratio of one radioisotope to the other. This limitation was taught in Claim 52 which was indicated by the examiner to be allowable when the rejection and objection are overcome.

Claim 93 rewords a limitation previously found in claim 61 which was rejected in light of Cotrell et al. Beta radiation should not be compared with ion beams because beta radiation occurs naturally. Using a magnetic field to focus ion beams are well known to those skilled in the art when those beams are generated for a specific purpose. Beta radiation has never been focused by any prior arts because such focusing serves no utility. In the case of the claimed invention, focusing beta radiation enables better resolution and more accurate detection that enhances the analysis. This is a newly founded utility that is non-obvious even though the methodology transition from focusing ion beam to beta radiation is obvious.

Applicant further request the examiner's assistant in writing new claims or rewriting existing claims that would put the application in condition for allowance.

Respectfully,
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